REMARKS

Claims 65-83 and 85-93 were pending in the Application. Claim 84 is not present due to misnumbering of the claims as amended on 08/10/2000. Upon entry of the present Amendment, claims 65-67, 69, 72-82, 85-91 are pending and presented for reconsideration. Applicants respectfully submit that no new matter is introduced by the present Amendment. A marked-up copy of the amended claims and a clean copy of the amended claims is attached herewith for the Examiner's convenience.

Support for the amendment to claim 65 may be found in the Specification at, for example, page 9, lines 17-27. The amendment does not introduce new matter and is made without any intention to abandon the subject matter as filed, but with the intention that claims of the same, greater, or lesser scope may be filed in a continuing application.

Acknowledgements

Applicants acknowledge that the Examiner has withdrawn the previous objections and rejections relating to:

(i) the disclosure, for a missing abstract;

(ii) the disclosure, for not referencing the OPCT Application;

(iii) the disclosure, for reciting the word "novel" in the title; and

(iv) all the outstanding rejections of claims 1-64, in view of the cancellation of claims 1-64.

Objections to the Claims

The Examiner objected to claim 73 for the misspelling of "domain". The typographical error has been corrected. Applicants therefore respectfully request that the objection be withdrawn.

The Examiner objected to claim 77 for using the word "or" in the Markush language. Applicants have amended the Markush language to recite "and". Applicants therefore respectfully request that the objection be withdrawn.

Rejection of Claims Under 35 U.S.C. §112, First Paragraph

The Examiner rejected claims 65-81 under 35 U.S.C. §112, first paragraph, stating that

> "[T]he specification, while being enabling for an isolated mouse osteoclastogen[e]sis inhibitory [factor] (OCIF) binding protein comprising the amino acid sequence set forth in SEQ ID NO:1 and an isolated human OCIF binding protein comprising the amino acid sequence set forth in SEQ ID NO:11, said polypeptide encoded by a polynucleotide comprising the nucleotide sequence set forth in SEQ ID NO:2 or SEQ ID NO:12 respectively, and a fragment of the polypeptide of SEQ ID NO:1 comprising amino acid residues 72-316 or 76-316, and a method of recombinantly making said polypeptides, is not enabling for "all" possible mouse or human purified osteoclastogenesis inhibitory [factor] (OCIF) binding proteins, or "all" soluble membrane proteins, or secreted mouse or human purified OCIF binding proteins, or "all" human or mouse OCIF binding proteins that lack the transmembrane domain or that are fused to a heterologous protein sequence, or fragments, analogs or variants of said proteins that bind to OCIF or promote osteoclast differentiation and maturation. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims."

In particular, the Examiner rejected claims 77 and 81, stating that the "[i]nstant specification is non-enabling for [a] polypeptide encoded by a nucleic acid sequence which hybridizes to the complement of SEQ ID NO: 2, 12, 15, 18 or 19, at the conditions recited in the claims, said polypeptide retaining its OCIF binding property, because the instant specification does not disclose said polypeptide" or that "there is no teaching or guidance that a nucleic acid sequence which hybridizes to the complement of SEQ ID NO: 2, 12, 15, 18 or 9 would encode a polypeptide that binds to OCIF." Applicants traverse the rejection to the extent it is maintained over the claims as amended.

An analysis of enablement requires a determination of whether that disclosure, when filed, contained sufficient information regarding the subject matter of the claims as to enable one skilled in the pertinent art to make and use the claimed invention. The test of enablement is whether one skilled in the art could make or use the claimed invention from the disclosures in the patent application coupled with information known in the art without undue experimentation.

United States v. Telectronics, Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343, 188 USPQ 659 (CCPA 1976). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation. *M.I.T. v. A.B. Fortia*, 774 F.2d 1104, 227 USPQ 428 (Fed. Cir. 1985).

Applicants have amended claim 77 to more clearly recite the limitation that the polypeptides encoded by the nucleic acids recited in the claims also bind to OCIF. Applicants respectfully point out that their specification not only discloses the protein and nucleic acid sequences of both mouse and protein homologs of OCIF binding protein, but further provides detailed guidance and specific protocols for isolating additional proteins and nucleic acids based on homology to these sequences (see pages 52-100 of Applicants' specification). These methods are also very well known in the art and are routinely used to screen genes and gene products from both the same and other species for additional homologs of genes and gene products once one nucleic acid sequence or polypeptide sequence has been identified. Given the redundancy of the genetic code, it is also the standard practice of the USPTO to provide to inventors of such sequences reasonable protection from others who can alter their sequences to avoid infringement by providing inventors with protection for highly similar sequences which are capable of hybridizing to their sequences under stringent hybridization conditions and which also retain the functionality of their sequences, in this case, the ability to bind to OCIF.

In addition, Applicants provide detailed protocols for making and using their claimed invention in the Examples on pages 52-144. In particular, Applicants' specification provides protocols for obtaining and characterizing OCIF-binding protein, including cultivating mouse osteoblastic stromal ST2 cells and preparation of membrane-bound proteins on pages 53-54; preparation of OCIF affinity columns and their use for the purification of OCIF-binding proteins of the invention on pages 54-56; methods for further purification of the OCIF-binding proteins of the invention by gel filtration and reverse phase high performance liquid chromatography on pages 56-57; and SDS-PAGE of the purified OCIF-binding proteins for determining the molecular weight of the OCIF-binding proteins on pages 57-58. In addition, pages 60-61 provide the standard protocols for testing the binding capacity of the OCIF-binding protein of the instant invention for

osteoblasts and pages 66-67 provide a protocol for determining the ability of the OCIF-binding proteins of the invention to bind to ^{125}I labeled OCIF by Scatchard Plot analysis. These methods can be employed to ensure that the proteins encoded by the nucleic acids of the invention retain the ability to bind to osteoblasts and to promote osteoclast differentiation and maturation, as is required by the claims.

Applicants also provide detailed protocols on pages 67-73 for constructing and screening expression libraries using methodologies in which OCIF-binding proteins are isolated by their ability to bind to the expression libraries. Briefly, DNA library pools were transfected into COS-7 cells and ^{125}I labeled OCIF was added to the cells to determine whether the transfected COS-7 cells expressed the transfected DNA encoding OCIF-binding protein (see Applicants' specification at page 70). Cells were then lysed and ^{125}I was measured to determine which of the COS-7 cells harbored DNA encoding OCIF-binding protein. These procedures, which are standard in the art, were then routinely repeated to isolate the individual cDNAs. Once cDNAs were obtained, they were further tested by expressing the protein encoded by the cDNA in COS-7 cells. Their ability to bind to OCIF was also confirmed by binding of ^{125}I-labeled OCIF to the transfected COS-7 cells. Thus, Applicants' specification provides more than ample guidance to enable one in the art to make, test and use the invention as claimed without undue experimentation.

The Examiner also rejected claims 70 and 71 under 35 U.S.C. §112, first paragraph, contending that "the specification does not provide the requisite examples nor a representative number of different sequences that would allow the skilled artisan to produce fragment[s] of the polynucleotide of SEQ ID NO:1 or 11 which retains it's ability to bind OCIF." In order to expedite prosecution of the case but not to acquiesce to the Examiner's rejection, Applicants have canceled claims 70 and 71. Applicants reserve the right to prosecute these and similar claims in continuation or divisional applications.

Rejection of Claims Under 35 U.S.C. §112, Second Paragraph

The Examiner rejected claims 64-76 under 35 U.S.C. §112, second paragraph, contending that the claims were indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner rejected claims 64-79, 81-91 for reciting the acronym "OCIF", without first reciting the full name of the protein in the first independent claim. Accordingly, applicants have amended claim 65 to recite "Osteoclastogenesis Inhibitory Factor (OCIF)".

The Examiner also rejected claim 83 for reciting "about 690bp". Claim 83 has been canceled, thereby rendering moot the examiner's rejection.

Applicants respectfully request that the rejections under 35 U.S.C. §112, second paragraph be withdrawn.

Rejection of Claims Under 35 U.S.C. § 102(e)

The Examiner rejected claims 69, 72-81, 85-91 35 U.S.C. §102(e) as being unpatentable over U.S. Patent 5,843,678 (hereinafter, "Boyle"). The Examiner asserts that the polynucleotide disclosed in Boyle shares 100% identity to SEQ ID No. 2 and encodes a polypeptide which is 100% identical to the polypeptide of SEQ ID NO 1.

Applicants respectfully traverse the rejection to the extent it is maintained over the claims as amended. Applicants' earliest effective priority for OCIF binding protein is to Japanese Patent Application 97808/1997, filed April 15, 1997, a certified English translation of which was provided to the U.S. Patent and Trademark Office with the filing of this Application on December 15, 1998 and acknowledged by the Examiner in the Office Action Summary Sheet mailed on February 25, 2000. In view of Applicants' perfection of their priority claim, the reference to Boyle cannot be properly applied with respect to the protein claims as amended and should be reconsidered and withdrawn. Applicants respectfully request that other matters relating to the Examiner's rejections over Boyle under 35 U.S.C.§102(e) be held in abeyance until all other rejections have been overcome.

The Examiner also rejected claims 69, 72-81, 85-91 under 35 U.S.C. §102(e), contending that it is anticipated by Anderson et al. (U.S. Pat, No. 6,017,729). Applicants respectfully request that the Examiner's rejections over Anderson et al. under 35 U.S.C.§102(e) be held in abeyance until all other rejections have been overcome.

Rejection of Claims Under 35 U.S.C. § 102(b)

The Examiner rejected claims 82 and 83 under 35 U.S.C. §102(b), contending that it was anticipated by Anderson et al. (11/97, i.e. Nature 390:175-179 (Nov. 13, 1997)). Applicants traverse the rejection. The Examiner has improperly cited this reference against Applicants. As the Examiner herself stated on pages 2-3 of the Office Action:

> "(b) 151434/1997 filed on 06/09/97 discloses mouse cDNA encoding OCIF binding molecule, and the full length mouse protein sequence. Claims drawn to mouse DNA and encoded protein get this priority date.
>
> (c) 217897/1997 filed on 08/12/97 discloses fragments of the mouse OBM 72-316, 76-316.
>
> (d) 224803/97 filed on 08/21/97 discloses human cDNA and encoded protein and fragments thereof. Claims to human DNA and encoded protein get this priority date.

The Anderson article was published in *Nature* on November 13, 1997, after the above quoted priority dates and is therefore not a proper reference under 35 U.S.C. §102(b), given the perfection of Applicants' priority claim. Applicants therefore contend that the rejection is improper and request that it be withdrawn.

CONCLUSION

Applicants submit that all claims as amended are allowable and respectfully request early and favorable action by the Examiner. If the Examiner believes that a telephone conversation with Applicants' agent would expedite prosecution of this application, the Examiner is cordially invited to call the undersigned.

Respectfully submitted,

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MARKED UP COPY OF THE AMENDED CLAIMS

65. (Once Amended) A purified and isolated Osteoclastogenesis Inhibitory Factor (OCIF) [OCIF] binding protein comprising a molecular weight of approximately 40,000 Daltons by SDS-PAGE, wherein said OCIF-binding protein promotes osteoclast differentiation and maturation.

69. (Once Amended) The OCIF-binding protein of claim 65 [or 68], comprising an amino acid sequence selected from the group consisting of SEQ ID NO. 1, SEQ ID NO. 11, SEQ ID NO. 16, and SEQ ID NO. 17.

73. (Once Amended) The OCIF-binding protein of claim 65, wherein said protein lacks a transmembrane domain [domane].

77. (Once Amended) A purified and isolated polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO. 2, SEQ ID NO. 12, SEQ ID NO. 15, SEQ ID NO. 18[,] and SEQ ID NO. 19, or a nucleic acid sequence which hybridizes at 2X SSC, 65°C to the complement of any of SEQ ID NO. 2, SEQ ID NO. 12, SEQ ID NO. 15, SEQ ID NO. 18, and SEQ ID NO. 19, and wherein said polypeptide [having] has the ability to bind OCIF.

78. (Once Amended) The OCIF-binding protein of claim 77, wherein said protein is a recombinant protein produced by [the] expression in a host cell.

81. (Once Amended) An isolated nucleic acid molecule capable of hybridizing in 2X SSC, 65°C to the complement of a nucleic acid sequence selected from the group consisting of [comprising] SEQ ID NO. 12, SEQ ID NO. 15, SEQ ID NO. 18, and SEQ ID NO. 19, and encoding a protein which binds to OCIF.

88. (Once Amended) The isolated nucleic acid of claim 80, wherein the protein encoded by said nucleic acid suppresses the biological activity of OCIF.

90. (Once Amended) The isolated nucleic acid of claim 80, wherein the protein encoded by said nucleic acid suppresses the biological activity of OCIF.

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